



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,452	10/14/2004	Paul Leslie Ornstein	X-15558	2319

25885 7590 07/25/2006

ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

EXAMINER

SEAMAN, D MARGARET M

ART UNIT	PAPER NUMBER
----------	--------------

1625

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

DETAILED ACTION

This application was filed 14 October 2004 and is 371 of PCT/US03/10466 (4/14/2003) which claims benefit of Provisional Application 60/376120 (4/26/2002). Claim 20 has been deleted. Claims 1-20, 22-23 and 26-40 are before the Examiner.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

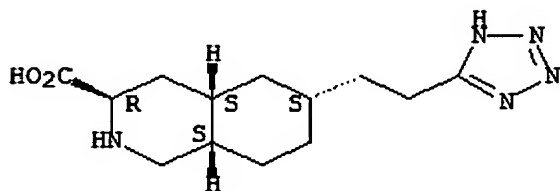
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-20, 22-23 and 26-40 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Salhoff in view of Bundgaard (WO 8801615). The rejection is maintained. As previously stated:

Salhoff teaches compounds such



as that are useful to treat pain. Salhoff does not teach the ester on the three position of the isoquinoline core.

Bundgaard teaches that ester derivatives of known compounds are prodrug formulations of carboxylic acid drug and provide improved bioavailability and are less irritating to the mucosa.

It would have been obvious to one of ordinary skill in the art to take a known drug, such as the above shown decahydroisoquinoline, and make an ester prodrug formulation with the reasonable expectation of getting a prodrug having better capabilities than the parent drug. Rationale: Bundgaard teaches the ester formulations of carboxylic acid drugs and Salhoff teaches the compound as a valuable drug.

Applicant argues that Bungdaard does not teach the use of the smaller ester prodrug formulations. However, Bundgaard teaches any and all ester prodrug formulations but has specific examples of the larger prodrug formulations. To show that the ordinary artisan knows of the smaller ester prodrug formulations, are Bundgaard (J of Med Chem, Vol 28, Number 8, August 1985, pp 979-981) that has alkyl and aralkyl esters of pilocarpic acid to correct a delivery problem with the original drug and Wang (Current Med Chem, Vol 7, pages 437-453, 2000) which makes simple ester

prodrugs to improve membrane permeability and oral activity. Bundgaard and Wang show that even the small prodrug formulations are known in the art of prodrug formulations as is taught by Bundgaard (WO 8801615).

Conclusion


4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 571-272-0694. The examiner can normally be reached on 730am-4pm, Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms